THE STRUCTURE OF THE SYNTHETIC α-POLYPEPTIDES

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The classic work of Astbury [1] has shown that structurally the fibrous proteins fall into two main groups: the keratin-myosin-epidermin-fibrinogen group, known for short as k-m-e-f, and the collagens. The distinction between them is displayed most clearly by their wide-angle X-ray diffraction patterns. These also show that the k-m-e-f group can exist in two forms, known as α and β, which under certain circumstances can be converted into each other. Astbury suggested many years ago that the β form corresponded to an extended configuration of the polypeptide chain, and that the α form contained chains folded so that their overall length was approximately halved. This explanation is now generally accepted as being correct, at least in outline.

In recent years it has been possible to prepare synthetic polypeptides in which all the sidechains are the same, and to study them by X-rays and infra-red rays. These too show a β, or extended, form and an α, or folded, form. The X-ray pattern of the latter is similar to but not identical with the α pattern of the k-m-e-f fibrous proteins.

Until 1951 the exact nature of the fold of the α-polypeptides was not known, although several configurations had been suggested. In that year a structure of a novel type, known as the α-helix, was proposed by Pauling, Corey and Branson [2]. Recent developments have left no doubt that this structure is basically correct.

The main object of the present article is to review the evidence in favour of the α-helix, and in particular to explain why it is considered correct although the agreement with the experimental evidence is not yet perfect. A brief description of the α-helix is given first to enable the reader to grasp the general nature of it.

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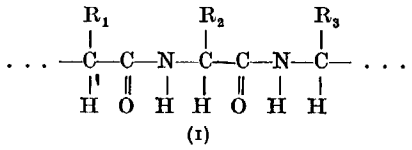
The α-helix was originally deduced by Pauling, Corey and Branson from a set of plausible stereochemical postulates, but it can also be derived independently from the broad features of the experimental evidence. *The strength of the case for the α-helix lies in the fact that both methods of approach give the same answer.* It is at first sight surprising that a structure of such apparent complexity can be solved at all, and the reasons why a solution can be obtained in this case are explained. Finally some of the lessons to be drawn from the history of the α-helix are pointed out, and the possible occurrence of the α-helix in proteins is briefly discussed.

The Polypeptide Chain

The basic formula of a polypeptide chain is shown in (I):



(I)

Here R_1, R_2, R_3 . . . represent the side groups. An average protein, of molecular weight 20,000, will contain nearly 200 of them. Only about twenty different *types* of side-groups are commonly found in proteins, and for all of them the configuration about the asymmetric carbon atom is L. (Glycine, which has no asymmetric carbon atom, since R is a hydrogen atom, is naturally an exception). The relative amounts in which these side-groups occur in some given protein is now known to a fair degree of accuracy for a large number of different proteins. However, with the exception of Sanger's epoch-making work on insulin, it has so far been impossible to establish the exact *sequence* of the residues in the polypeptide chains of any natural protein.

In a synthetic polypeptide the side-groups, R, are usually all the same, although co-polymers, in which two or more side-groups occur at random, have also been prepared. An average chain contains some hundreds of residues. The nature of the side-groups is of course not restricted to the twenty types found in natural proteins, nor need the residues have the L configuration. The polypeptides are usually prepared by the Leuchs' reaction. The fold which they take up on precipitation depends to a considerable extent on the solvent from which they are cast. Oriented specimens, usually in the form of thin films, can be obtained by a variety of techniques, such as stroking the material with a razor blade during

precipitation. These films can then be examined by X-rays and by polarised infra-red rays. The great body of the experimental work in this field, with one important exception, has been done by workers in the laboratories of Courtaulds Limited [3, 4, 5, 6, 7].

The chemical formula shown in (I) is not enough by itself to fix the structure—the configuration of the molecule in space. This is because rotation is possible about single bonds, and therefore, in theory, a large number of configurations are possible. Nevertheless the X-ray photographs show clearly that a unique structure exists.

Description of the α-Helix

The α-helix is a configuration for the backbone of the polypeptide chain. Of the atoms of the side-group it only fixes the position of the one directly connected to the polypeptide backbone. The remaining atoms, which depend upon the particular polypeptide being studied, are not located by the general model.

In the α-helix each repeating unit of the backbone is related to its neighbour by a screw axis coinciding with the fibre axis. The novel feature of the α-helix is that the screw axis is a non-integer one. In a three-dimensional crystal a screw (or rotation) axis must be 2-, 3-, 4- or 6-fold, but for a single chain such a restriction is not essential, and the screw for the α-helix is (approximately) an advance of 1·5 Å and a rotation of 100°. Thus there are 3·6 residues in 360°, and the structure only repeats exactly, in the crystallographic sense, after 18 residues and 5 turns.

This type of arrangement is shown symbolically in Fig. 1. The general run of the polypeptide chain is shown by a continuous helical wire, and the repeating sequence of atoms is symbolised by a series of small spheres placed on the wire, one sphere representing one group of atoms. The crystallographic repeat occurs when one sphere is *exactly* above one lower down (taking the fibre axis as vertical). It is easy to see that the distance of this repeat is not a very characteristic feature of the α-helix, since if the structure is twisted very slightly the exact repeat is

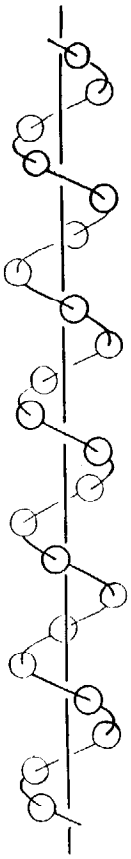


FIG. 1.—A non-integer helix having 3·6 groups per turn. Each group of atoms is symbolised here by a ball.

destroyed. The approximate parameters of the screw (1·5 Å and 100°) are more fundamental characteristics, since a small deformation only changes them slightly.

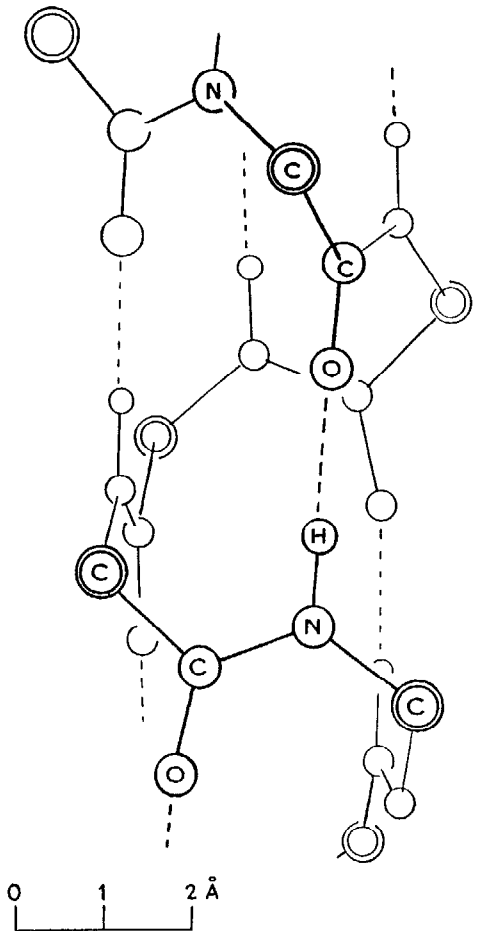


FIG. 2.—A projection of part of an α-helix.
Only the backbone atoms are shown. The side-groups join on to the carbon atoms represented by the double circles. Hydrogen bonds are dotted.

The structure takes up this configuration because of the way in which it is held together. This is done by hydrogen bonds between the NH of one residue and the O of the residue near to it on the next turn of the helix. The hydrogen bonds are approximately parallel to the fibre axis, and form struts linking adjacent turns

of the helix together. In Fig. 2, which shows a projection of a small part of the α-helix, the hydrogen bonds are shown dotted.

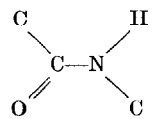
The basic reason why the polypeptide chain forms a non-integer helix, rather than one with a crystallographic axis, is that the structure is dominated by the interaction between successive turns of the same helix, rather than by interactions between adjacent helices. The screw axis applies only to the residues of one chain. It does not relate neighbouring helices to each other.

THE DERIVATION OF THE α-HELIX

The α-helix was derived by Pauling, Corey and Branson [2] by enumerating a series of postulates and then searching systematically for all those configurations which satisfied them. These postulates were :

(1) normal bond distances and angles for chemical bonds,
(2) the planarity of the peptide (amide) bond,
(3) good hydrogen bonding,
(4) equivalence.

The great strength of this type of method really lies in the first postulate. Largely due to the careful work of the crystallographers at the California Institute of Technology [8] there has been built up over the past fifteen years an accurate body of information on the probable bond distances and angles of the polypeptide chain. This has been obtained by studying small molecules, such as amino acids and peptides. A structure which deviated from these distances by more than about 5 per cent., or from the angles by more than a few degrees would be regarded as very unlikely. The second and third postulates also derive from this work. The short length of the C—N bond (1·32 Å), indicating partial double-bond character, and the fact that in all the crystals so far examined the peptide group (II)



(II)

has been planar, or very nearly so, strongly supports this postulate. Similarly a set of empirical rules for NH . . . O hydrogen bonds can be given (Donohue [9]). For example the N . . . O distance should not be far from 2·85 Å, and the N—H bond should point approximately towards the oxygen atom.

The fourth postulate is of a radically different type. By "equivalence" one means that an atom in one residue has an identical atomic environment to the corresponding atom in any other residue —the configuration of one residue is "equivalent" to any other residue. For a chain containing asymmetrical carbon atoms (making mirror and glide planes impossible) this necessarily implies a screw axis of symmetry between one residue and the next. This postulate therefore defines a class of structures. Another class, for example, would consist of structures in which the asymmetric unit (upon which the screw acts) contained not one residue, but a pair of adjacent residues. The tacit assumption that the unit of structure (of the folded polypeptide) was a single polypeptide chain, and not, for example, a pair of chains wound helically together, also further restricts the class to be examined.

There was also an additional assumption that the peptide configuration was *trans* and not *cis*. This is reasonable, since all the small molecules so far examined which could take up either form have been found to be *trans*.

It is a feature of such a set of postulates (as first realised by Kendrew) that one can enumerate *topologically* all possible structures that can fulfil them. In effect the hydrogen bond completes a ring of atoms, and one can enumerate all possible rings that a polypeptide chain could form. While in theory there are an infinite number of them, it can easily be shown that the larger rings give quite impossible structures, and in practice only the lower members need be considered.

Pauling, Corey and Branson suggested that only two types of helix were possible: the α-helix, and a wider helix which they named the γ-helix. Pauling and Corey [10] later put forward subsidiary reasons why the γ-helix was unlikely, and some additional arguments in favour of the α-helix. The problem has recently been re-examined by Donohue [11]. He took each possible helix in turn and built it in the very best form he could, not insisting too precisely on the exact fulfilment of the postulates, but adjusting each structure so that the overall deviation from the optimum conditions was a minimum. He was thus able to show that a number of other helices were not impossible, but that by every test the α-helix configuration was the best. The importance of this work is that we are sure that no simple helix has been overlooked.

Such a result is very suggestive, but it is certainly not enough in itself to establish a structure, and we must now turn to the experimental evidence and see how far this leads us without any recourse to postulates or careful model building.

The Infra-Red Evidence

It is convenient to consider the infra-red evidence first. The frequencies mainly examined were the C—O vibrations in the 6μ region, and the N—H vibrations in the 3μ region. These show clearly that the great majority of the NH groups are forming hydrogen bonds. Moreover, if the α-form is dissolved, the character of the infra-red absorption is unchanged even at great dilutions [4]. This suggests that the hydrogen bonds are formed within the structural unit, and that this unit persists in solution.

Polarised infra-red studies, mainly by Elliott [4], showed that the dichroism of these bands in favourable specimens of the α-polypeptides was high, and occasionally very high, and in such a sense that the hydrogen bonds were (approximately) parallel to the fibre axis. This in itself would show that the polypeptide chain was not fully extended in the fibre direction.

X-Ray Fibre Diagrams

The X-ray pictures obtained are fibre diagrams. This means that the crystallites which make up the specimen have been aligned so that the polypeptide chains are all roughly parallel, while the orientation of the crystallites about the fibre axis is random, or nearly so. The effect on the X-ray photograph is the same as if a single crystallite had been rotated about its fibre axis while the photograph was being taken. Thus all (or almost all) the information is superposed on one photograph, which is rarely an advantage. For example, when the lattice is exactly hexagonal in shape this means that every reflexion observed is in reality a number of different reflexions superposed, due to the random orientation of the crystallites. This naturally reduces the amount of information that one can obtain.

The lack of exact parallelism between the fibre axes of the crystallites, which draws out the spots into arcs, various forms of disorder in the crystallites, and the amorphous material inevitably present in the specimen all reduce the precision of the data, and in general fibre diagrams compare poorly with X-ray photographs of single crystals.

A further loss of information can occur if the specimen is not tilted to obtain the wide-angle reflexions near the meridian. This technique is almost as old as X-ray crystallography, but it was neglected in this field before the work of Perutz [12].

The quality of the X-ray photographs obtained varies from

specimen to specimen. The recent pictures obtained by the Courtaulds workers [6, 7] are of an extremely high technical quality, and this goes some way to offset the inherent disadvantages of fibre diagrams. The quality also depends to some extent on the particular polypeptides under examination. The best pictures have been given by poly-γ-methyl-L-glutamate and, more recently, by poly-L-alanine, and the following remarks apply mainly to them.

The X-Ray Evidence

In the first place the unit cell is hexagonal in shape, as shown by careful measurements of the reflexions on the equator of the X-ray diagram and the well-defined row lines. (The glutamate shows signs of a double cell, but this does not alter the argument.) It is thus possible, from the measured density, to compute the average length in the fibre direction corresponding to one residue, and this comes to about $1\frac{1}{2}$ Å. This suggests that there can only be one chain in the crystallographic unit, since the α configuration can be extended to about twice its length to give the β form, the maximum possible extension of which is 3·7 Å. If there were two chains per lattice point, and thus one residue *per chain* in every 3 Å, it would not be possible to extend the structure to twice its length. The first order equatorial reflexion is very strong, showing that there is a concentration of atoms not far from the fibre axis. These very general considerations suggest that the structural unit consists of a single polypeptide chain, held together by hydrogen bonds parallel to the fibre axis and not deviating from it by more than 2 Å or 3 Å.

So far the features described have been rather commonplace, but the next feature of the X-ray diffraction pattern is very remarkable. It is found that the minimum size of the unit cell required to explain all the layer-lines is no less than 27 Å long in the fibre direction. Thus the crystallographic unit must contain a large number of chemical repeats. To offset this apparent complexity, a great number of the X-ray reflexions are absent, or at least too weak to observe. In fact whole layer-lines are missing. This implies that within the 27 Å cell there must be a high degree of regularity.

As another possible approach one might consider only those layer-lines on which reflexions are observed to occur. It is then found that these can best be indexed using *two* parameters instead of the usual one. For a normal unit cell of length 27 Å the spacings of the successive layer-lines would be submultiples of 27. That is, the lth layer-line would correspond to a spacing (in the fibre direction) of $27/l$ Å, or, as a crystallographer would prefer to say, the reciprocal spacings are multiples of $l/27$ Å^{-1}. Now for the polypeptide unit cells the reciprocal spacings of the *observed* layer-lines can all be fitted to an expression of the form

$$\frac{n}{5{\cdot}4} + \frac{m}{1{\cdot}5}$$

where m and n are *small* integers, positive or negative. If now the layer-line spacings are measured very carefully, it is found that a 27 Å cell is not long enough to index them accurately, and that a cell 43 Å or even 103 Å in length is required. Nevertheless a rule of the form, say,

$$\frac{n}{5{\cdot}43} + \frac{m}{1{\cdot}497}$$

accounts for the observed layer-lines exactly. This clearly needs some explanation.

The other general feature of the X-ray pattern is that the reflexions on the meridian apart from one or two very weak ones are all absent, with the exception of one very strong reflexion at 1·497 Å, originally discovered by Perutz [12]. Of the remaining layer-lines the strongest is that with spacing about 5·4 Å. There is only one reasonable interpretation of these features. The structure must be based on a helix of pitch distances 5·4 Å having a residue every 1·5 Å in the fibre direction. It was shown by Cochran and Crick [13] that such a structure would lead to precisely the features described. One might expect on general grounds that it would show both the 5·4 and the 1·5 periodicities and also the "side-bands" of the one periodicity on the other, and this proves to be the case.

The theory predicts that on any given layer-line the X-ray reflexions near the meridian will be weak or absent unless n (in the formula given above) is small. The larger n is, the larger the size of the empty region of the diffraction pattern. This is exactly what is found for the synthetic α-polypeptides.

We can now ask, how many structures can be built to fit these broad features of the infra-red and X-ray data? It can be shown (Trotter, unpublished) that making only the broadest stereochemical assumptions there are only two possible structures. One of these is so awkward that more refined model building shows it to be extremely unlikely. The other is the α-helix. This rough model building also shows, as surmised earlier on other grounds, that structures based on two intertwined polypeptide chains are impossible.

We have thus arrived at the α-helix by two distinct routes. Firstly by very careful model-building to a set of plausible postulates. Secondly from considering the general features of the experimental evidence. Thus even without calculating a single structure factor a strong case can be made for the α-helix.

Difficulties

A detailed comparison of the X-ray intensities (Bamford *et al.* [5, 7]) shows that the equatorial intensities agree perfectly with the α-helix, but when the rest of the experimental data is studied carefully certain difficulties emerge. The intensities of the general reflexions are in fair but not perfect agreement with the calculated values. In particular there are weak "forbidden" reflexions on the meridian. This probably means that the α-helix is distorted. It is also not clear exactly how the side-chains pack in those polypeptides in which they are rather long. This difficulty does not arise with poly-L-alanine [7], in which R is a single methyl group, and in this case the helix is almost certainly slightly deformed due to the effects of neighbouring helices. Non-integer helices are awkward things to pack together. A good fit at one point invariably produces a bad fit somewhere else. This packing difficulty probably also explains the fact that the observed density is rather on the high side. The ordered part of the structure, from the dimensions of which the calculated density is obtained, is probably a rather open pack, and may be less dense than the less-ordered regions. This is true, for example, of ice and water.

There is a further complication in that the α-helix is not perfectly defined. Although not stated above, it is really two possible structures, not one. Even though all the asymmetric carbon atoms have the L-configuration the structure can be built in two ways, depending upon whether the helix is made right-handed or left-handed. As far as the actual backbone of the polypeptide chain is concerned they are mirror images of each other, but the points of attachment of the side-chains are not related in this way, and the two structures are therefore distinct. It is not clear whether one of these forms predominates, or whether there is usually a mixture, either ordered or random.

Finally, the infra-red dichroism, while agreeing qualitatively with the α-helix, shows quantitative discrepancies. Some of these are probably due to an orbital-following effect, as suggested by Price and Fraser [14].

Why a Solution is possible

We therefore have the somewhat odd situation that, though the structure has not been proved in the strict crystallographic manner, it is nevertheless almost certainly correct in outline. To see how this has come about it is useful to look at the problem again from a more unified viewpoint. Let us first assess the general character of the problem. Even assuming a unit cell only 27 Å long, there will be at least 90 atoms in it, not counting the distal parts of the side-chains nor the hydrogen atoms. The experimental data, by comparison with that from a single crystal, is rather poor, and in particular there are few spacings shorter than $2\frac{1}{2}$ Å. At first sight it could reasonably be concluded that there was little hope of solving the structure.

What transforms the situation is the existence of the screw axis. What would normally be accepted as evidence for a screw axis? For a six-fold screw, for example, one would require six-fold symmetry of the intensities in the reciprocal lattice and the absence of all meridional reflexions, excepting every sixth one. This evidence is essentially statistical in nature. The argument really states that, while the observed intensities could in theory be due to chance, the odds against such an explanation are extremely high. The argument for the non-integer screw in the α-polypeptides is of exactly the same character. In this case one cannot observe the symmetry of the intensities because this is concealed by the fact that the X-ray picture is a fibre diagram. The expected absences, on the other hand, are much more numerous, and the difficulty of indexing the layer-lines exactly using a single parameter gives additional support to the helical interpretation. It is not possible, for example, to explain the layer-lines as being due to two structures of the normal type existing simultaneously in the specimen.

Once the argument for the non-integer screw has been accepted, the number of backbone atoms whose co-ordinates one has to determine falls from 90 to 5. But this is not all, because the 15 parameters needed to fix their position are by no means independent. The most important restriction, and one that does not occur with small molecules, is that, being a polymer, each set of five atoms is joined at both head and tail to one of its neighbours. This reduces enormously the possible configurations. If we now allow ourselves to assume the normal bond angles and distances, we find that only three parameters are required to define the structure completely. These are the angles of rotation about the three single bonds in the repeating unit of the chain. If in addition we make

the peptide bond planar, since the presumptive evidence for this is very strong, only two parameters are necessary. Moreover, because of the hydrogen-bonding the two angles cannot take all values, but are restricted to a small number of possibilities. It is thus not surprising that the problem, at first sight so difficult, can be solved approximately.

What complicates the situation is that the structure of the α-helix is systematically distorted and that it is by no means clear how many parameters are needed to characterise the distortion. The present claim, however, is that the α-helix, in one or both of its forms, is the *basis* of the structure. Moreover, due to the difficulties of packing, some small distortion is to be expected.

The Identification of a Helix

What lessons can be drawn from the history of the work on the α-helix ? In the first place we are now conscious of the possibility of non-crystallographic and non-integer helices. If the layer-lines of a fibrous structure do not index easily using a single parameter the structure is probably a non-integer helix. Again, the regions of absent or weak reflexions predicted by the helical diffraction theory may be immediately obvious, as in the recent work on DNA (desoxyribonucleic acid) by Wilkins [15], Franklin [16] and their colleagues. On other occasions a more subtle pattern of absences may be formed, such as that noticed by Watson [17] in X-ray photographs of Tobacco Mosaic Virus. The helical diffraction theory [25, 26] is now an essential tool for anyone wishing to study the diffraction effects of a fibrous structure.

Model Building

The second lesson to be drawn is the importance of careful model building, and in particular of building models with as few preconceived ideas as possible. It must be remembered that when Pauling, Corey and Branson devised the α-helix the experimental evidence was much less complete than it is to-day. In particular, the strong 1·5 Å reflexion on the meridian, so dramatically predicted and discovered by Perutz [12] in poly-benzyl-L-glutamate, was then unknown, and there was little to suggest the existence of a non-integer helix. Pauling and Corey insisted on the planarity of the peptide bond, but this was only important because previous workers had quite inexcusably overlooked it. Their really novel contribution was to suggest that the screw axis need not be integer. It is worth while examining why this point was missed by Bragg, Kendrew and Perutz [18], who had previously attempted to discover the fold by systematically building models. In their case, however, they were trying to fit the model to the data for the fibrous proteins. These show a strong reflexion at 5·15 Å *on the meridian*, and this does indeed suggest an integer screw axis. We now know that this feature is misleading. Thus, not only is the method of building scale models an extremely powerful one, since it embodies a large amount of data which any successful model must include, but for structures of this type it may well pay to build models without giving much attention to the experimental evidence. It is not going too far to state that, at the stage where model building is usually first attempted, some of the experimental evidence then available will usually turn out at a later date to be wrong, or at least deceptive. There is a case, in fact, for careful model building independent of most of the experimental data.

Enthusiasm for this type of approach should not blind one to its limitations. It is likely to be successful where the X-ray diagram shows features which suggest considerable regularity, and in particular where the experimental evidence, for reasons of technical difficulty, is less trustworthy than one might hope. It is especially suitable for regular fibres, because of the restriction that the monomer units must be joined head to tail, which is particularly easy to incorporate in a scale model. Among biological material those that spring to mind are the fibrous proteins, the nucleic acids and the nucleoproteins. On the other hand, it is not yet clear whether this method will prove of any value for the globular proteins.

In the last analysis there is no substitute for good experimental work, since no structure can be proved without it, but if the correct solution is guessed, or guessed in outline, experience shows that the experimental work proceeds more efficiently This is usually true in all fields, but it is particularly true in crystallography.

Occurrence in Synthetic Polypeptides

Finally a few words should be said about the general occurrence of the α-helix. It is noteworthy that *every* synthetic folded polypeptide so far examined gives the same sort of X-ray pattern, although it is sometimes very disordered. In all cases a strong 1·5 Å reflexion is observed on the meridian, and this may be taken as presumptive evidence for the presence of an α-helix—but the reflexion must be strong, and it must be in this special position. Perhaps one should also add that the material must be known to contain polypeptide chains !

It is, in fact, a little surprising that so far no trace has been

found of any of the other possible helices, since they are energetically not so very much less favourable than the α-helix. It happens that these other helices are all members of the same "family"—that is, they can be transformed from one to another without completely unwinding the polypeptide chain. For example, models suggest that one can start to build a π-helix (a somewhat wider helix discovered by Dr. Barbara Low [19]) and then change over to building an α-helix. At the point where the change occurs in the structure only one hydrogen bond is unmade. The model suggests that this unmade bond could move from place to place in one direction making more π-helix, in the other direction making more α-helix. (It could move, that is, in the sense that a "hole" in a crystal is said to move.) Eventually, since the α-helix is energetically preferable, the join would run off the end and the chain would be all α-helix. In other words, a π-helix can probably change into an α-helix by a process involving a low activation energy. This might explain why the other helices have so far not been spotted in synthetic polypeptides.

Occurrence in Proteins

What of the fibrous α-proteins, such as α-keratin, the protein of hair and horn? McArthur [20] originally observed the 1·5 Å reflexion in African Porcupine quill, but its crucial importance was overlooked. It has since been found in all the folded members of the k-m-e-f group. It is a strong reflexion, but probably not as strong as in the synthetic polypeptides. However, instead of the layer-line at 5·4 Å the α-proteins give a *meridional* reflexion at 5·15 Å, which would not be expected for an α-helix parallel to the fibre axis. Tilting the α-helix is not enough by itself, as this would throw the 1·5 Å reflexion away from the meridian.

The observed pattern has now been tentatively explained as due to α-helices inclined and slowly coiling round each other, either because of repeating sequences of residues (Pauling and Corey [21]) or because non-integer helices might be expected on general packing grounds to go together in this way (Crick [22, 23]). Such structures can be shown to give both the 5·15 Å *and* the 1·5 Å reflexions on the meridian. They also explain two other weaker meridional reflexions and the general nature of the reflexions on and near the equator of the X-ray diagram. It can no longer be claimed that the α-keratin pattern cannot be interpreted in terms of the α-helix. It still remains to be established that this explanation is correct, and to work out the details of the structure, which is in any case likely to be more complicated than this simple picture.

As to the globular proteins, the key molecules of molecular biology, it is at the moment a matter of opinion how valuable the α-helix is going to be in unravelling their structure. It is certain that globular proteins do not consist entirely of α-helices arranged strictly parallel to one another, or their structure would have been found long ago. How much, if any, of their polypeptide chains are coiled in the α-helix configuration remains to be discovered.

The α-helix, then, is the basis of the structure of the folded synthetic polypeptides. It is probably the basis of the fibrous α-proteins. It may be an important feature of the globular proteins. One can readily agree with Edsall [24] who has written "... the formulation of the α-helix seems to me to be one of the great creative triumphs of thinking in the field of protein chemistry."

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